

REMARKS

Claims 88-116 are currently pending in this application. Claims 91, 93, 94, and 105-116 are withdrawn from examination as allegedly drawn to unelected inventions. Claims 88 and 108 are amended. Support for those amendments can be found throughout the specification, *e.g.*, at page 8, lines 7-10, page 9, lines 6-9, page 40, lines 12-14, page 42, lines 19-22, page 64, lines 1-10, and the section titled "Coupling" on pages 125 through 132. Thus, no new matter has been added. Applicant respectfully requests the entry of these amendments under 37 C.F.R. § 1.116.

I. WITHDRAWN REJECTIONS

Applicant notes that the Office has not maintained the following rejections in the current Office Action:

- The rejection of claims 88-90, 92, and 95-104 under 35 U.S.C. § 112, ¶ 2 as allegedly indefinite;
- The rejection of claims 88-90, 92, 95, 96, and 98-103 under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,610,022 to Battifora ("*Battifora*");
- The rejection of claim 97 under 35 U.S.C. § 103 as allegedly obvious over *Battifora* in view of Harvey Lodish, *Molecular Cell Biology* 4th Ed. §§ 17.5, 23.4, and 23.7 (W. H. Freeman and Company 1986) (2000) ("*Lodish*");
- The rejection of claim 104 under 35 U.S.C. § 103 as allegedly obvious over *Battifora* in view of O'Leary T.J., "Standardization in Immunohistochemistry," *Applied Immunohistochemistry & Molecular Morphology*, 9:3-8 (2001) ("*O'Leary*"); and
- The provisional obviousness-type double patenting rejection of claims 88-90, 92, 95, 96, and 98-104 as allegedly unpatentable over claims 1-26, 31, 33-40, 44, 45, and 48-52 of copending U.S. Patent Application No. 11/884,247 alone, or in view of *O'Leary*.

Accordingly, Applicant assumes these rejections have been withdrawn. (*See also* Office Action at p. 2.)

II. REJECTIONS UNDER 35 U.S.C. § 102

Claims 88, 92, 95, 96, 98-100, and 102-104 are rejected under 35 U.S.C.

§ 102(b) as allegedly anticipated by EP 0345953 to Cosgrove et al. ("*Cosgrove*"). (See Office Action at pp. 3-4). Specifically, the Office contends:

Cosgrove et al. teach a standard for use as a positive quantitative control (i.e., reference standard) comprising pellets of an absorbent gel (i.e., compact particles), where specific concentrations of an antigen of interest are adsorbed and confined in the pellets (i.e., comprising a quantity of detectable entity attached to the particle). ... Cosgrove et al. further teach that the pellets may be embedded into a gel block (i.e., support medium ...).

(*Id.* at p. 3.) The Office also rejects claim 97 as allegedly anticipated by *Cosgrove* in light of Hood et al., "Unravelling the proteome of formalin-fixed paraffin-embedded tissue," Briefings in Functional Genomics and Proteomics, 5(2):169-75 (2006) ("*Hood*"). (See Office Action at pp. 4-5.) Specifically, the Office contends that "Hood et al. provide evidence that the process of formalin fixation results in various combinations of intra- and inter-molecular covalent crosslinks between proteins, RNA and DNA ..." (*Id.*)

Without acquiescing to these rejections, and solely to facilitate prosecution, claim 88, from which claims 92, 95, 96, 97, 98-100, and 102-104 depend, is amended to recite "wherein at least one dimension of the compact particle is less than 1500 μm ," i.e., less than 1.5 mm. In contrast, *Cosgrove*'s gel pellets are 5 mm in depth (column 6, lines 39-42) and 2.5 or 1.5 mm in diameter (column 6, line 56 through column 7, line 2). Accordingly, *Cosgrove* cannot anticipate the instant invention because it fails to expressly or inherently teach each and every limitation set forth in the currently amended claims. (See M.P.E.P. § 2131, 8th Ed., July 2008 Rev.)

For at least these reasons, Applicant respectfully requests that the Office withdraw the rejections of claims 88, 92, 95, 96, 97, 98-100, and 102-104 under 35 U.S.C. § 102(b).

III. REJECTIONS UNDER 35 U.S.C. § 103

Claims 88-90, 92, and 95-103 are rejected under 35 U.S.C. § 103 as allegedly obvious over *Battifora* in view of U.S. 2002/0127205 to Edge (“*Edge*”). (See Office Action at pp. 5-8). The Office acknowledges that *Battifora* “does not specifically teach a reference standard in which the compact particles do not express the detectable entity” (*id.* at page 6), but contends that *Edge* cures this deficiency in *Battifora* by teaching that “a protein can be chemically crosslinked to a cell surface using commercially available crosslinking reagents” (*id.*). The Office also rejects claim 104 as allegedly obvious over *Battifora* in view of *Edge* and further in view of *O’Leary*. The Office acknowledges that *Battifora* and *Edge* fail “to specifically teach the inclusion of a positive control that comprises a compact particle with substantially no detectable entity” (Office Action at page 9), but contends that *O’Leary* cures this deficiency by allegedly teaching “that the interpretation of immunohistochemical stains should be guided by the staining of appropriate positive, negative, and internal controls whenever possible” (*id.*). Applicant respectfully traverses.

“To reach a proper determination under 35 U.S.C. § 103, the Examiner must step backward in time and into the shoes worn by the hypothetical ‘person of ordinary skill in the art’ when the invention was unknown and just before it was made.” M.P.E.P. § 2142, 8th Ed., July 2008 Rev. Applicant respectfully submits that the Office has failed to establish a *prima facie* case of obviousness of claims 88-90, 92, and 95-104 because

the alleged motivation to modify *Battifora* requires impermissible hindsight based on the teachings of the instant specification.

As discussed previously, *Battifora* does not expressly or inherently teach “[a] reference standard for a detectable entity ... comprising a compact particle ... wherein the compact particle does not express the detectable entity,” as required by claim 88, from which claims 89-90, 92, and 95-104 depend. (See Response dated May 4, 2009, at p. 8.) Instead, as the Office acknowledges, *Battifora* focuses solely on reference standards that are genetically modified to express a detectable entity. (See Office Action at pp. 5-6; and *Battifora* at col. 2, ll. 3-24, col. 3, ll. 12-43, col. 4, ll. 1-3, and Examples 1-3.) *Battifora* recognizes no shortcomings in such reference standards and, therefore, provides no motivation to modify the reference standards by “chemically crosslinking antigens to the surfaces of cells, rather than ... introducing genetic material,” as alleged on page 7 of the Office Action.

Edge and *O’Leary* fail to cure this deficiency in *Battifora*, since neither reference describes any relevant standardization system having features that could be combined with *Battifora*’s system, and neither reference discusses any advantages from using reference standards having antigens chemically crosslinked to the surfaces of cells. *O’Leary* merely discusses the advantages of using reference standards having weak reactivities (see paragraph bridging pages 5-6), and *Edge* does not discuss reference standards at all. Instead, *Edge* relates solely to modified cells for use in avoiding immune rejection during transplantation. (See, e.g., *Edge* at abstract and [0006].)

Since the combinations of references cited by the Office fail to identify any shortcomings with the reference standards disclosed in *Battifora*, one skilled in the art

would have had no reason to modify such reference standards based solely on *Edge's* disclosure that isolated proteins may be coupled to cells (see [0099]). In fact, the inventors were the first to recognize the significant problems associated with reference standards that express detectable entities and to identify viable solutions. (See specification at p. 5, ll. 21-31 and p. 7, ll. 2-6.) Accordingly, the instant invention would not have been obvious to one skilled in the art because the prior art failed to recognize any reason to arrive at the claimed invention.

For at least these reasons, Applicant respectfully requests that the Office withdraw the rejection of claims 88-90, 92, and 95-104 under 35 U.S.C. § 103.

IV. DOUBLE PATENTING REJECTION

Claims 88-90, 92, and 95-104 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-32 and 35-41 of copending U.S. Patent Application No. 10/547,033 ("the '033 application") in view of *Battifora* and *Edge*. (See Office Action at pp. 10-11.) Applicant respectfully traverses.

As the Office acknowledges, claims 1-32 and 35-41 of the '033 application do not recite "[a] reference standard ... comprising ... a quantity of detectable entity attached to [a] compact particle, wherein the compact particle does not express the detectable entity," as recited in the currently pending claims. For the reasons discussed above, *Battifora* and *Edge* also do not teach or suggest these elements of the instant invention and, therefore, fail to cure the deficiencies in the '033 application. Thus, the Office has not established a *prima facie* case of provisional obviousness-type double patenting because one of skill in the art cannot arrive at the instantly claimed invention merely by

combining claims 1-32 and 35-41 of the '033 application with the teachings of *Battifora* and *Edge*.

For at least these reasons, Applicant respectfully requests that the Office withdraw the provisional double patenting rejection of claims 88-90, 92, and 95-104.

V. REJOINDER

In view of the amendments and arguments presented herein, Applicant respectfully submits that the elected invention of reference standards and the elected species of cells are allowable over the prior art. Thus, in accordance with 37 C.F.R. §§ 1.104 and 1.141, Applicant respectfully requests that the Office rejoin the withdrawn process claims and extend examination to the unelected species of compact particles to the extent necessary to find the generic claims allowable.

CONCLUSION

Applicant respectfully requests entry of Amendment under 37 C.F.R. § 1.116, placing claims 88-116 in condition for allowance, for at least the following reasons: (1) the Final Office Action presented new prior art rejections against Applicant's invention and, therefore, entry of this Amendment would allow Applicant to reply to the new rejections and place the application in condition for allowance; and (2) entry of the amendment would place the application in better form for appeal, should the Examiner continue to dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicant submits that this claimed invention, as amended, is neither anticipated nor rendered obvious by of the prior art references cited against this application. Applicant therefore requests the entry of this Amendment,

the Examiner's reconsideration of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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